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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/018,170 | 12/11/2001 | Henry Yue | PF-0733 USN | 8478 |

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| EXAMINER | |
|---|---|
| STEADMAN, DAVID J | |
| ART UNIT | PAPER NUMBER |
| 1652 | |

DATE MAILED: 12/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Advisory Action | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/018,170 | YUE ET AL. | |
| | Examiner | Art Unit | |
| | David J Steadman | 1652 | |

*--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

THE REPLY FILED FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1.☒ A Notice of Appeal was filed on *27 October 2003*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2.☐ The proposed amendment(s) will not be entered because:

(a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

(b) ☐ they raise the issue of new matter (see Note below);

(c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

(d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____.

3.☐ Applicant's reply has overcome the following rejection(s): _____.

4.☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5.☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *see attachment*.

6.☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7.☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: _____.

Claim(s) rejected: *205,206,208,209,211-215,217,224-226 and 228-231*.

Claim(s) withdrawn from consideration: *219-223*.

8.☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9.☐ Note the attached Information Disclosure Statement(s)( PTO-1449) Paper No(s). _____.

10.☐ Other: _____

## ADVISORY ACTION

**[1]** Claims 205-206, 208-209, 211-215, 217, 219-226, and 228-231 are pending in the application.

**[2]** Claims 219-223 remain withdrawn from consideration as being drawn to a non-elected invention.

**[3]** Claims 205-206, 208-209, 211-215, 217, 224-226, and 228-231 stand finally rejected.

**[4]** The amendment to the claims filed August 29, 2003 has been entered into the record. This listing of the claims replaces all prior versions and listings of the claims.

**[5]** The request for reconsideration is acknowledged, however the amendment does not place the application in condition for allowance for the reasons stated below.

**[6]** Applicants' request for rejoinder of claims 208-209 as being drawn to methods of use of the claimed polypeptide and claims 219-223 as allegedly being drawn to methods of use of the claimed polynucleotide (see page 8 of the August 29, 2003 amendment) is acknowledged. It is noted that claims 208-209 are being examined in the instant application and have been rejoined in a previous Office action (see item 6 of the Office action mailed June 30, 2003). Regarding rejoinder of claims 219-223, as the polynucleotide claims are not in a condition for allowance, rejoinder is not yet required.

**[7]** In view of applicants' amendment to the title and cancellation of claims 207 and 216, the objections set forth in items 9 and 10 of the Office action mailed June 30, 2003 are withdrawn.

**[8]** The rejection of claims 205-206, 208-209, 211-215, 217, 224-226, and 228-231 under 35 U.S.C. 101 and 112, first paragraph (see item 11 of the Office action mailed June 30, 2003) is maintained for the reasons of record. Regarding gene expression analysis, applicants argue they do not need to demonstrate differential expression of the claimed polynucleotide – only whether the polynucleotide is useful. Applicants argue well-established uses, such as toxicology testing and drug screening need not be described in the specification. Applicants argue the Bedilion Declaration demonstrates that a skilled artisan, in light of the specification, would have understood the use of SEQ ID NO:64 in gene expression analysis. Applicants' argument is not found persuasive.

In this case, applicants have not demonstrated a specific and substantial utility for the claimed polynucleotide as the specification provides no guidance to allow a skilled artisan to use data relating to the claimed polynucleotides derived from the results of toxicology testing and what the results would mean. For example, if the claimed polynucleotides were attached to a microarray and used in toxicology testing or drug screening analysis and a result showed that expression was increased when a cell was treated with a particular agent, the specification provides no basis on which a skilled worker would be able to determine whether that result is meaningful. As such, further experimentation would be required to interpret the results of such gene expression analysis.

Applicants argue there need not be a correlation between the claimed polynucleotide and a disease in order for the polynucleotide to be useful in disease diagnosis as each individual sequence has utility in creating arrays and has a unique

and specific utility in that it records expression level. Applicants argue that measuring the expression level of the claimed polynucleotide for toxicology testing would not require knowledge of biological function or disease association. Applicants argue that every expressed human polynucleotide has specific utility in toxicology testing. Applicants' argument is not found persuasive.

Applicants' statement that all sequences have a utility as recording gene expression supports the argument that this is not a specific utility as the use of a polynucleotide for measuring expression can be applied to the broad class of polynucleotides. If any polynucleotide expressed in a human has utility in toxicology testing, then that polynucleotide has no *specific* utility as all polynucleotides would have such use, regardless of the dependence on the identity of a given polynucleotide and therefore, does not satisfy the utility requirement of 35 USC § 101. In a related example, all polynucleotides have use for protein expression. The encoded amino acid sequence for any given nucleic acid is specific and dependent upon the identity, i.e., nucleotide sequence, of the encoding nucleic acid. However, as *all* nucleic acids have utility for protein expression, this utility is not specific and therefore does not satisfy the utility requirement of 35 USC § 101.

Applicants argue the claimed polynucleotide has use as a control in toxicology testing, which is shared by the large class of polynucleotides. Applicants argue the issue is whether the invention has any utility not whether other compounds have a similar utility. Applicants argue nothing in the law says that an invention must have a "unique" utility and that the whole notion of "well-established" utility presupposes that

many different inventions can have the exact same utility. Applicants argue that if the examiner's argument were correct, there could never be a "well-established" utility.

It is noted that applicants have never been asked to identify a utility that is unique, i.e., not shared by any other compounds or compositions. Rather, applicants are required to identify a utility that is specific to the invention claimed, as opposed to one that would apply regardless of the specific properties of the claimed invention. An invention certainly can have a utility that is shared by other compounds or compositions. On the other hand, not every utility will satisfy 35 USC § 101, even if the utility is shared by a class of inventions. So while a utility need not be unique to a claimed invention, it must nonetheless be specific, and in currently available form, in order to satisfy § 101.

Applicants argue because SEQ ID NO:12 shares 99.7% identity to pemphaxin, SEQ ID NO:12 is pemphaxin and is a member of the annexin family of proteins. Applicants' argument is not found persuasive.

There is no dispute that SEQ ID NO:12 shares a high degree of sequence identity to another annexin. However, this alone does not indicate that SEQ ID NO:12 has annexin biological activity as there is no functional assay of the protein of SEQ ID NO:12 that would verify the protein has biological activity – it is just as likely that the protein is a non-functional mutant of pemphaxin. Also, it is unclear to the examiner as to how SEQ ID NO:12, which is structurally distinct from pemphaxin can – at the same time – be pemphaxin. While two compounds may be structurally similar, this does not make them identical, as asserted by applicants. In this case, because SEQ ID NO:12 is

structurally distinct from pemphaxin, one of skill in the art would recognize that SEQ ID NO:12 cannot be pemphaxin.

Applicants argue that because SEQ ID NO:12 is pemphaxin, it can be used in the diagnosis and treatment of autoimmune disorders. Applicants' argument is not found persuasive.

As stated above, it is unclear as to how SEQ ID NO:12 can be pemphaxin. Also, as the specification provides no guidance for using SEQ ID NO:12 for diagnosing or treating an autoimmune disorder, further experimentation would be required to determine which, if any, autoimmune disorder(s) SEQ ID NO:12 is/are so useful in diagnosing and treating and if SEQ ID NO:12 is so useful, how to use SEQ ID NO:12 for diagnosing and treating an autoimmune disorder.

Applicants argue other members of the annexin family display calcium-dependent and calcium independent binding of phospholipids. Applicants argue that, as a member of the annexin family, SEQ ID NO:12 is likely to be a phospholipid binding protein and is useful as a cell marker. Applicants' argument is not found persuasive.

As stated above, there is no evidence of record, including applicants' cited references, that would indicate that SEQ ID NO:12 has functional activity, particularly phospholipid binding activity – it is just as likely that the protein is a non-functional mutant of pemphaxin. In the absence of such evidence, applicants have failed to demonstrate that SEQ ID NO:12 has such utility and further experimentation would be required to determine if SEQ ID NO:12 can be used as cell markers. Even assuming *arguendo* that the specification demonstrated phospholipid binding activity of SEQ ID

NO:12, the specification provides no guidance for using SEQ ID NO:12 as a cell marker, thus requiring further experimentation for such use.

Applicants argue that in view of the Furness Declaration, a skilled artisan would have understood the uses of the claimed polypeptide in protein expression monitoring. Applicants argue the examiner does not dispute the use of SEQ ID NO:12 in 2-D PAGE gels and western blots in drug toxicity monitoring and contends that the polypeptide cannot be useful without knowledge of its function. Applicants' argument is not found persuasive.

The examiner agrees that, along with any other protein, SEQ ID NO:12 can be used in 2-D PAGE gels and western blots in drug toxicity monitoring – this non-specific use applies to the broad class of proteins. Furthermore, the specification provides no guidance to allow a skilled artisan to use data relating to the claimed polypeptide derived from the results of toxicity testing and what the results would mean. For example, if the expression of the claimed polypeptide were monitored in a drug toxicity test, the specification provides no basis on which a skilled worker would be able to determine whether that result is meaningful. As such, further experimentation would be required to interpret the results of such expression analysis.

Applicants argue the claimed proteins are useful as tools for toxicology testing, drug discovery, and the diagnosis of disease and that these uses are "well-established". Applicants cite the references of Rockett et al. (*Xenobiotica* 29:655), Nuwaysir et al., Steiner et al., Rockett et al. (*Environ Health Perspectives* 107:681), and an email from Dr. Cynthia Afshari to an Incyte employee, and examples (as set forth at the bottom of

page 16 of the appeal brief) that allegedly support their assertions. Applicants' argument is not found persuasive.

In this case, the specification fails to provide the necessary guidance for using the claimed polypeptide for toxicology testing, drug development, and disease diagnosis. Any polypeptide can be used for expression analysis for toxicology testing and the specification fails to provide guidance regarding the interpretation of data derived from such a test. Furthermore, the specification fails to disclose the use of the claimed polypeptide for drug development and fails to provide guidance regarding any disease that can be diagnosed using the claimed protein.

**[9]** The enablement rejection of claims 205-206, 208-209, 211-215, 217, 224-226, and 228-231 under 35 USC 112, first paragraph (see item 14 of the Office action mailed June 30, 2003), is maintained for the reasons of record and the reasons stated below. Applicants argue the instant rejection fails for the reasons presented in addressing the rejection under 35 USC 101. Applicants' argument is not found persuasive. The examiner maintains that the claimed invention lacks patentable utility and is not enabled for the reasons of record and those stated above.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (703) 308-3934. The Examiner can normally be reached Monday-Friday from 7:00 am to 5:00 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX number for submission of official papers to Group 1600 is (703) 308-4242. Draft or informal FAX communications should be directed to (703) 746-5078. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

David J. Steadman, Ph.D.
Art Unit 1652

Rebecca Prather

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